UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

NOV 15 2005

MEMORANDUM

SUBJECT: Registration of Milsana Bioprotectant Concentrate (EPA File Symbol No.072179-E) an End-use product containing 5% Reynoutria sachalinensis, also known as Giant knotweed: Chemical No. 055809; Case No. 065909: Review of Toxicological Studies. Submission No. S565442; MRID Nos. 448219-05,-07,-08, -10, -12 ,and -14; DP Barcode No. D257774

FROM: Freshteh Toghrol, Ph.D., Senior Scientist F. Toghrol
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division

TO: Driss Benmhend, Team Leader
Microbial Pesticides Branch
Biopesticides & Pollution Prevention Division

ACTION REQUESTED

KHH BioSci, Inc., requests registration of Milsana Bioprotectant Concentrate (EPA File Symbol No 072179-E) containing 5% Reynoutria sachalinensis, also known as giant knotweed.

To support this registration the registrant has submitted the following mammalian toxicological studies: an acute oral toxicity study in rats (MRID No. 448219-05), an acute dermal toxicity in rats (MRID No. 448219-07), an acute inhalation study in rats (MRID No. 448219-08), a primary eye irritation study in rabbits (MRID No. 448219-10), a dermal irritation study in rabbits (MRID No.448219-12),and a dermal sensitization study in guinea pig (MRID No. 448219-14).

BPPD'S CONCLUSIONS AND RECOMMENDATIONS

Based on toxicological data submitted by the registrant, BPPD has no objection to the registration of an end-use product Milsana Bioprotectant Concentrate (EPA File Symbol No.072179-E) containing 5% Reynoutria sachalinensis (Giant knotweed).

STUDY SUMMARIES

152-10 An Acute Oral Toxicity Study in Rats (MRID 448219-05)

Based on the data submitted by the registrant, the acute oral LD_{50} of Milsana Bioprotectant Concentrate is greater than 5000 mg/kg in rats. The test material was administered at a dose of 5000 mg/kg body weight to groups of five male and five female Albino rats. The animals were observed for signs of toxicity three times on the day of dosing and daily thereafter for 14 days. One female died on day 1, all other treated rats survived. On the day of dosing, hypoactivity and impaired muscle coordination were noted from one male, one surviving female and the female that died during the study. Three males had yellow to brown color around the mouth or urogenital area on dosing day to day one. All surviving rats recover by day 2 and had normal body weight gains. On gross necropsy the female rat that died had pale kidneys and dark red stomach content. There were no test material related clinical finding, all rats that survived gained weight during the test period. No significant changes were observed for gross necropsy in nine of ten animals. Classification: Acceptable, Toxicity Category IV.

152-11 An Acute Dermal Toxicity Study in Rats (MRID 448219-07)

Five male and five female rabbits received a single dose of 2000 mg/kg body weight of Milsana Bioprotectant Concentrate. After 24 hours of exposure, the acute dermal LD_{50} was found to be greater than 2000 mg/kg body weight in male and female New Zealand white rabbits. All animals survived through the 14 day observation period, all rats had normal body weight gain, and no treatment related clinical signs were observed. Very slight erythema was noted on four males and one female on day 1 and 2 and on one female on days 3 and 4. Desquamation was noted on all males and three females from days 3-9. One female had desquamation on days 11 and 12, exfoliation on day 13, and focal eschar on days 13 and 14. No gross necropsy finding were observed.

Classification: Acceptable, Toxicity Category III.

152-12 Acute Inhalation Toxicity Study in Rats (MRID No. 448219-08)

Five males and five females rats were exposed for 4 hours to the test substances under the following conditions: oxygen content of chamber air 20%, chamber air changes/hour: at least 12

Chamber Environment	
Chamber Volume	130 L
Airflow	26.3 LPM
Temperature	22±0.3°C
Relative Humidity (mean)	68±13.3%

Chamber Atmosphere		
Gravimetric Concentration	**MMAD [a]**	**GSD**
2.6 mg/L	3.5 μm	2.54

[a]Approximately 56% of particles had an aerodynamic diameter ≤ 4.0 μm

Exposure Concentration mg/L	Number of Deaths/Number Tested		
	Males	Females	Combined
2.6	0/5	0/5	0/10

No rats died during the study. No toxicologically significant clinical signs were noted during exposure and the observation period. Dark brown material covered the entire body of all rats on days 1 and/or 2. Two males had an unkempt appearance on days 3-5 and 3-9, respectively. Three males had swollen/scabbing ears and/or wet red material on right lateral neck toward the end of the second week. With the exception of three females that lost weight during the first week and one female that did not gain weight during the second week, all rats gained weight during the study. No gross findings were observed. LC_{50} (mg/L): > 2.6 mg/L,

Classification Acceptable, Tox. Category IV

152-13 Primary Eye Irritation Study in Rabbits (MRID 448219-10)
Three males and 3 females rabbits were given a dose of 0.1 ml of test substances.

Observations	Number "positive"/number tested							
	Hours				Days			
	1	24	48	72	4	7	14	21
	Unwashed eyes							
Corneal Opacity	4/6	2/6	1/6	1/6	1/6	1/6	1/6	0/6
Iritis	5/6	1/6	1/6	1/6	1/6	1/6	0/6	0/6
Conjunctivae:								
Redness	2/6	4/6	1/6	1/6	1/6	1/6	0/6	0/6
Chemosis	6/6	3/6	1/6	1/6	1/6	1/6	0/6	0/6
Discharge	6/6	1/6	1/6	0/6	0/6	0/6	0/6	0/6

The Draize method for scoring eye irritation was used. Three rabbits had corneal opacity one hour after instillation of the test material with resolution on two rabbits by 24 hours and on one rabbit by 48 hours. Iritis was noted on 4/6 and 1/6 rabbits at 1 and 24 hours, respectively. Five rabbits had positive conjunctivitis one hour after test material instillation with resolution by 48 hours. One male rabbit had corneal opacity one hour after test material instillation that persisted through day 14 with resolution by day 21, had irits at 1, 48, and 72 hours and days 4 and 7 with resolution by day 14, and had positive conjunctivitis one hour after test material instillation through day 7. This male rabbit had corneal epithelial damage, peeling and corneal neovascularization. One female had corneal epithelial damage, peeling at 24 hours. The highest average ocular irritation index was 23.3 recorded 1 hour after initiation. This classifies the test material as moderately irritating. Toxicity Category: II

Classification: Acceptable,; Toxicity Category: II

152-14 Primary Dermal Irritation Study In Rabbits(MRID 448219-11)

Four hours of exposure to a single dose of 0.5 grams of Milsana Bioprotectant Concentrate to six rabbits (3 each sex) produced very slight erythema in one rabbit at 48 hours (by Draize method), with resolution by 72 hours. Yellow staining observed on the application sites of all animals there was no edema, or any other dermal findings. The primary irritation Index was calculated to be 0.0, which is non-irritation.

Classification: Acceptable, Toxicity Category IV.

152-15 Buehler Sensitization Study In Guinea Pigs(MRID 448219-14)

In a preliminary irritation test, undiluted test material was determined to be appropriate for induction and challenge dosing. The animals were induced and challenged according to the modified Buehler method. The backs and flanks of 20 male and 20 female guinea pigs were clipped on the day prior to each dosing. For the induction phase, 0.4 mL of the undiluted test material was applied under occlusion for six hours once each week for three weeks. Two weeks after the third induction, the animals were challenged with 0.4 mL of undiluted test material under occlusion at naive sites for 6 hours. A naive control group was treated with 0.4 mL of undiluted test material at challenge only. The positive control group animals were induced with 0.4 mL of undiluted HCA and challenged with 0.4 mL of 50% w/v HCA in acetone. A naive positive control group was challenged with 0.4 mL of 50% w/v HCA in acetone at challenge. Reactions were scored 24 and 48 hours post exposure. Slight patchy erythema was noted on 2/20 and 1/20 test animals 24 and 48 hours, respectively, after the first induction, on 5/20 and 2/20 test animals 24 and 48 hours, respectively, after the second inductions, and on 3/20 test animals 24 hours after the third induction. No reaction was noted on any test animal after challenge. Slight patchy erythema was noted on 2/10 naive control animals 24 hours after challenge. The positive control and positive naive control animals responded appropriately.

There is no indication that this product is a dermal sensitizer. Classification: Acceptable.

Acute Mammalian Toxicity of Milsana Bioprotectant Concentrate (EPA File Symbol 072179-E) containing 5% Reynoutria Sachalinensis as its active ingredient ; Lot AF-455-79-1 [a]

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity rat/WIL Research Laboratories, Inc., WIL-349007/12-8-98	448219-05	LD_{50} > 5000 mg/kg	IV	A
Acute dermal toxicity rat/WIL Research Laboratories, Inc., WIL-349008/12-8-98	448219-07	LD_{50} > 2000 mg/kg	III	A
Acute inhalation toxicity rat/WIL Research Laboratories, Inc., WIL-349012/2-19-99	448219-08	LC_{50} > 2.6 mg/L	IV	A
Primary eye irritation rabbit/WIL Research Laboratories, Inc., WIL-349010/12-8-98	448219-10	Corneal opacity on 4/6 rabbits with resolution on two rabbits by 24 hours, on one rabbit by 48 hours, and on one rabbit by day 21; iritis on 5/6 and 1/6 rabbits at 1 and 24 hours, respectively, and one 1/6 rabbits from 48 hours through day 7 with resolution by day 14; positive conjunctivitis on 6/6 rabbits with resolution by day 14.	II	A
Primary dermal irritation rabbit/WIL Research Laboratories, Inc., WIL-349009/12-8-98	448219-12	Very slight erythema noted on 1/6 rabbits 48 hours after patch removal with resolution by 72 hours.	IV	A
Dermal sensitization guinea pig/WIL Research Laboratories, Inc., WIL-349011/12-8-98	448219-14	Not a sensitizer	--	A

Core Grade Key: A = Acceptable

cc: Driss Benmahand, F. Toghrol, BPPD Subject File.
F. Toghrol: F.T. CSF #1: (703) 308-7014: 11/15/99

DATA EVALUATION REPORT

MILSANA BIOPROTECTANT CONCENTRATE AND END-USE PRODUCT (MILSANA BIOPROTECTANT CONCENTRATE FORMULATED PRODUCT)

STUDY TYPES: ACUTE ORAL TOXICITY - RAT (81-1), MRID 44821905
ACUTE DERMAL TOXICITY - RAT (81-2), MRID 44821907
ACUTE INHALATION TOXICITY - RAT (81-3), MRID 44821908
PRIMARY EYE IRRITATION - RABBIT (81-4), MRID 44821910
PRIMARY DERMAL IRRITATION - RABBIT (81-5), MRID 44821912
DERMAL SENSITIZATION - GUINEA PIG (81-6), MRID 44821914

SUMMARY: ACUTE TOXICITY ONE-LINERS (81-1 through 81-6)

Prepared for

Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
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Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
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Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 30

Primary Reviewer:
Susan Chang, M.S. Signature: Date: NOV 0 3 1999

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T. Signature: Date: NOV 0 3 1999

Robert H. Ross, M.S., Group Leader Signature: Date: NOV 0 3 1999

Quality Assurance:
Donna L. Fefee, D.V.M. Signature: Date: NOV 0 3 1999 for D.L. Fefee

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§152-10, 870.1100)

EPA Reviewer: Freshteh Toghrol, Ph.D. E. Toghrol Date 11/15/99
Biopesticides and Pollution Prevention Division (7511C)

Study Title: Acute Oral Toxicity Study of Milsana bioprotectant Concentrate (Formulated Product) in Albino Rats

MRID No.: 448219-05
File Jacket Symbol: 072179-E
DP Barcode: D257774
Study No.: WIL-349007
Study Completion Date: December 8, 1998

Sponsor: KHH BioSci, Inc., P.O. Box 13169, 2 Davis Drive, Research Triangle Park, NC 27709
Testing Facility: WIL Research Laboratories, Inc., 1407 George Road, Ashland, OH 44805-9281
Author: Kern, T.G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Milsana bioprotectant Concentrate (Formulated Product, 5% w/v Milsana, a.i.); Lot AF-455-79-1; black opaque liquid
PC Code: 055809

Species: Rats; Albino, Crl:CD® (SD)IGS BR
Age: 11-13 weeks
Weight (fasted):5 Males: 325-364 g; 5Females: 227-249 g
Source: Charles River Laboratories, Inc., Raleigh, NC
Housing: Individually housed in suspended wire-mesh cages
Identification: Eartag
Food: PMI Nutritional Inc. Certified Roden LabDiet 5002
Water: Tap water
Temperature: 71.6-72.1 F
Humidity: 46.1-61.8%
Photoperiod: 12 hours light/dark cycle
Acclimation: 7 days
Procedural Deviations from Subdivision M Guideline §152-10: None

The test material was administered as received by oral gavage.

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	1/5	1/10

Observations: The test animals were observed for clinical signs at approximately 1, 3, and 4 hours post dosing on day 0 and twice daily thereafter for 14 days. One female was found dead on day 1. On the day of dosing, hypoactivity and impaired muscle coordination were noted from one male, one surviving female, and the female that died during the study. Three males had wet and/or dried yellow to brown material around the mouth or urogenital area on days 0 to 1. All surviving rats recovered by day 2 and had normal body weight gains.

Gross Necropsy: The decedent female had pale kidneys and dark red stomach contents. No gross necropsy findings were observed from the surviving rats.

Conclusion:

1. **LD_{50} (mg/kg):** > 5000 mg/kg
2. **Tox. Category:** IV
3. **Classification:** Acceptable

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§152-11, 870.1200)

EPA Reviewer: Freshteh Toghrol, Ph.D. F. Toghrol Date 11/15/99
Biopesticides and Pollution Prevention Division (7511C)

Study Title: Acute Dermal Toxicity Study of Milsana bioprotectant Concentrate (Formulated Product) in Albino Rats

MRID No.: 448219-07
File Jacket Symbol: 072179-E
DP Barcode: D257774
Study No.: WIL-349008
Study Completion Date: December 8, 1998

Sponsor: KHH BioSci, Inc., P.O. Box 13169, 2 Davis Drive, Research Triangle Park, NC 27709
Testing Facility: WIL Research Laboratories, Inc., 1407 George Road, Ashland, OH 44805-9281
Author: Kern, T.G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Milsana Bioprotectant Concentrate (Formulated Product, 5% w/v Milsana, a.i.); Lot AF-455-79-1; black opaque liquid
PC Code: 055809

Species: Rats; Albino, Crl:CD® (SD)IGS BR
Age: Young adult
Weight: 5 Males: 227-270 g; 5 Females: 217-243 g
Source: Charles River Laboratories, Raleigh, NC
Housing: Individually housed in suspended wire-mesh cages
Identification: Eartag
Food: PMI Nutritional Inc. Certified Roden LabDiet 5002
Water: Tap water
Temperature: 71.5-72.1 F
Humidity: 50.2-62.6%
Photoperiod: 12 hours light/dark cycle
Acclimation: 7 days
Procedural Deviations from Subdivision M Guideline §152-11: None

The test material was applied evenly to the shaved and abraded skin (approximately 16-20% of the body surface) and the test site semi-occluded for 24 hours.

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: The test animals were observed for clinical signs at approximately 1, 3, and 4 hours post dosing on day 0 and twice daily thereafter for 14 days. No clinical signs of toxicity were observed. All rats had normal body weight gains. Very slight erythema was noted on four males and one female on days 1 and 2 and on one female on days 3 and 4. Desquamation was noted on all males and three females from days 3 to 9. One female had desquamation on days 11 and 12, exfoliation on day 13, and focal eschar on days 13 and 14.

Gross Necropsy: No significant changes were observed.

Conclusion:

1. **LD_{50} (mg/kg):** > 2000 mg/kg
2. **Tox. Category:** III
3. **Classification:** Acceptable

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§152-12, 870.1300)

EPA Reviewer: Freshteh Toghrol, Ph.D. F. Toghrol Date 11/15/99
Biopesticides and Pollution Prevention Division (7511C)

Study Title: Acute Inhalation Toxicity Study of Milsana (Formulated Product) in Albino Rats

MRID No.: 448219-08
File Jacket Symbol: 072179-E
DP Barcode: D257774
Study No.: WIL-349012
Study Completion Date: February 19, 1999

Sponsor: KHH BioSci, Inc., P.O. Box 13169, 2 Davis Drive, Research Triangle Park, NC 27709
Testing Facility: WIL Research Laboratories, Inc., 1407 George Road, Ashland, OH 44805-9281
Author: Ulrich, C.E.

Quality Assurance (40 CFR §160.12): Included

Test Material: Milsana (Formulated Product, BAS 114 UB F); Lot AF455-79-1; black opaque liquid
PC Code: 055809

Species: Rats; Crl:CD®(SD)IGS BR VAF/PLUS®
Age: Males: Approximately 8 weeks; Females: Approximately 10 weeks
Weight: 5 Males: 283-294 g; 5 Females: 232-239 g
Source: Charles River Laboratories, Stoneridge, NY
Housing: Individually housed in suspended wire-mesh cages
Identification: Eartag
Food: PMI Nutritional Inc. Certified Roden LabDiet 5002
Water: Tap water
Temperature: 70-73 F
Humidity: 41-64%
Photoperiod: 12 hours light/dark cycle
Acclimation: 7 days

Procedural Deviations from Subdivision M Guideline §152-12: The relative humidity of the exposure chamber (68±13.3%) exceeded that required (40-60%).

Exposure Chamber: Whole body glass and stainless-steel chamber

Exposure: 4 hours

- Oxygen content of chamber air: 20%
- # Chamber air changes/hour: at least 12

Chamber Environment	
Chamber Volume	130 L
Airflow	26.3 LPM
Temperature	22±0.3°C
Relative Humidity (mean)	68±13.3%

Chamber Atmosphere		
Gravemetric Concentration	**MMAD [a]**	**GSD**
2.6 mg/L	3.5 μm	2.54

[a]Approximately 56% of particles had an aerodynamic diameter ≤ 4.0 μm.

Exposure Concentration mg/L	Number of Deaths/Number Tested		
	Males	**Females**	**Combined**
2.6	0/5	0/5	0/10

Clinical Observations: No rats died during the study. No toxicologically significant clinical signs were noted during exposure and the observation period. Dark brown material covered the entire body of all rats on days 1 and/or 2. Two males had an unkempt appearance on days 3-5 and 3-9, respectively. Three males had swollen/scabbing ears and/or wet red material on right lateral neck toward the end of the second week. With the exception of three females that lost weight during the first week and one female that did not gain weight during the second week, all rats gained weight during the study.

Gross Necropsy Findings: No gross findings were observed.

Conclusion:

1. **LC_{50} (mg/L):** > 2.6 mg/L
2. **Tox. Category:** IV
3. **Classification:** Acceptable

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§152-13, 870.2400)

EPA Reviewer: Freshteh Toghrol, Ph.D. F. Toghrol Date 11/15/99
Biopesticides and Pollution Prevention Division (7511C)

Study Title: Acute Eye Irritation Study of Milsana bioprotectant Concentrate (Formulated Product) in Albino Rabbits

MRID No.: 448219-10
File Jacket Symbol: 072179-E
DP Barcode: D257774
Study No.: WIL-349010
Study Completion Date: December 8, 1998

Sponsor: KHH BioSci, Inc., P.O. Box 13169, 2 Davis Drive, Research Triangle Park, NC 27709
Testing Facility: WIL Research Laboratories, Inc., 1407 George Road, Ashland, OH 44805-9281
Author: Kern, T.G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Milsana bioprotectant Concentrate (Formulated Product, 5% w/v Milsana, a.i.); Lot AF-455-79-1; black opaque liquid
PC Code: 055809
Dosage: 0.1 mL placed into the cupped lower conjunctival sac of the right eye of each test animal

Species: Rabbits; New Zealand White
Age: Young adult
Weight: 3 Males: 2782-3149 g; 3 Females: 2907-3151 g
Source: Covance Research Products, Inc., Denver, PA
Housing: Individually housed in suspended wire-mesh cages
Identification: Eartag
Food: PMI Nutritional Inc. Certified Roden LabDiet 5322
Water: Tap water
Temperature: 66.0-67.3 F
Humidity: 38.0-64.4%
Photoperiod: 12 hours light/dark cycle
Acclimation: 7 days

Procedural Deviations from Subdivision M Guideline §152-13: None

Observations	Number "positive"/number tested							
	Hours				Days			
	1	24	48	72	4	7	14	21
	Unwashed eyes							
Corneal Opacity	4/6	2/6	1/6	1/6	1/6	1/6	1/6	0/6
Iritis	5/6	1/6	1/6	1/6	1/6	1/6	0/6	0/6
Conjunctivae:								
Redness	2/6	4/6	1/6	1/6	1/6	1/6	0/6	0/6
Chemosis	6/6	3/6	1/6	1/6	1/6	1/6	0/6	0/6
Discharge	6/6	1/6	1/6	0/6	0/6	0/6	0/6	0/6

Results: The Draize[1] method for scoring eye irritation was used. Three rabbits had corneal opacity one hour after instillation of the test material with resolution on two rabbits by 24 hours and on one rabbit by 48 hours. Iritis was noted on 4/6 and 1/6 rabbits at 1 and 24 hours, respectively. Five rabbits had positive conjunctivitis one hour after test material instillation with resolution by 48 hours. One male rabbit had corneal opacity one hour after test material instillation that persisted through day 14 with resolution by day 21, had irits at 1, 48, and 72 hours and days 4 and 7 with resolution by day 14, and had positive conjunctivitis one hour after test material instillation through day 7 This male rabbit had corneal epithelial damage, peeling and corneal neovascularization. One female had corneal epithelial damage, peeling at 24 hours. The highest average ocular irritation index was 23.3 recorded 1 hour after initiation. This classifies the test material as moderately irritating.

Conclusion:

1. **Toxicity Category:** II
2. **Classification**: Acceptable

[1]Draize scale for scoring ocular lesions, as published in the guidelines in Subdivision F. Hazard Evaluation: Human and Domestics Animals distributed in 1984 and the OECD Guidelines for Testing of Chemicals distributed in 1987.

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (§152-14, 870.2500)

EPA Reviewer: Freshteh Toghrol, Ph.D. F. Toghrol Date 11/15/99
Biopesticides and Pollution Prevention Division (7511C)

Study Title: Acute Dermal Irritation Study of Milsana bioprotectant Concentrate (Formulated Product) in Albino Rabbits

MRID No.: 448219-12
File Jacket Symbol: 072179-E
DP Barcode: D257774
Study No.: WIL-349009
Study Completion Date: December 8, 1998

Sponsor: KHH BioSci, Inc., P.O. Box 13169, 2 Davis Drive, Research Triangle Park, NC 27709
Testing Facility: WIL Research Laboratories, Inc., 1407 George Road, Ashland, OH 44805-9281
Author: Kern, T.G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Milsana bioprotectant Concentrate (Formulated Product, 5% w/v Milsana, a.i.); Lot AF455-79-1; black opaque liquid
PC Code: 055809
Dosage: 0.5 mL of test material was applied to clipped, unabraded skin
Species: Rabbits; New Zealand White
Age: Young adult
Weight: 3 Males: 2865-3194 g; 3 Females: 2944-3250 g
Source: Covance Research Products, Inc., Denver, PA
Housing: Individually housed in suspended wire-mesh cages
Identification: Eartag
Food: PMI Nutritional Inc. Certified Roden LabDiet 5322
Water: Tap water
Temperature: 66.5-72.0 F
Humidity: 38.1-56.2%
Photoperiod: 12 hours light/dark cycle
Acclimation: 7 days

Procedural Deviations from Subdivision M Guideline §152-14: None
Results: The Draize[1] method was used for scoring the results. Very slight erythema was noted on 1/6 rabbits by 48 hours with resolution by 72 hours. PDIS = 0.0 (Non-irritating).

Conclusion:
1. **Toxicity Category**: IV
2. **Classification**: Acceptable

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[1]Draize, J.H., The Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. Dermal Toxicity, pp. 46-59. Assoc. of Food and Drug Officials of the U.S., Topeka, Kansas.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§152-15, 870.2600)

EPA Reviewer: Freshteh Toghrol, Ph.D. F. Toghrol Date 11/15/99
Biopesticides and Pollution Prevention Division (7511C)

Study Title: Skin Sensitization Study of Milsana bioprotectant Concentrate (Formulated Product) in Albino Guinea Pigs

MRID No.: 448219-14
File Jacket Symbol: 072179-E
DP Barcode: D257774
Study No.: WIL-349011
Study Completion Date: December 8, 1998

Sponsor: KHH BioSci, Inc., P.O. Box 13169, 2 Davis Drive, Research Triangle Park, NC 27709
Testing Facility: WIL Research Laboratories, Inc., 1407 George Road, Ashland, OH 44805-9281
Author: Kern, T.G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Milsana bioprotectant Concentrate (Formulated Product, 5% w/v Milsana, a.i.); Lot AF455-79-1; black opaque liquid
PC Code: 055809
Positive Control Material: α-Hexylcinnamaldehyde (HCA)

Species: Guinea pigs; Albino, Hartley Crl:(HA)BR
Age: Young adult
Weight: 20 Males: 292-364 g; 20 Females: 287-333 g
Source: Charles River Laboratories, Raleigh, NC
Housing: Individually housed in suspended wire-mesh cages
Identification: Eartag
Food: PMI Nutritional Inc. Certified Roden LabDiet 5026
Water: Tap water
Temperature: 71.7-72.3 F
Humidity: 40.3-57.4%
Photoperiod: 12 hours light/dark cycle
Acclimation: 7 days

Procedural Deviations from Subdivision M Guideline §152-15: None

Procedure: In a preliminary irritation test, undiluted test material was determined to be appropriate for induction and challenge dosing. The animals were induced and challenged according to the modified Buehler method. The backs and flanks of 20 male and 20 female guinea pigs were clipped on the day prior to each dosing. For the induction phase, 0.4 mL of the undiluted test material was applied under occlusion for six hours once each week for three weeks. Two weeks after the third induction, the animals were challenged with 0.4 mL of undiluted test material under occlusion at naive sites for 6 hours. A naive control group was treated with 0.4 mL of undiluted test material at challenge only. The positive control group animals were induced with 0.4 mL of undiluted HCA and challenged with 0.4 mL of 50% w/v HCA in acetone. A naive positive control group was challenged with 0.4 mL of 50% w/v HCA in acetone at challenge. Reactions were scored 24 and 48 hours post exposure.

Results: Slight patchy erythema was noted on 2/20 and 1/20 test animals 24 and 48 hours, respectively, after the first induction, on 5/20 and 2/20 test animals 24 and 48 hours, respectively, after the second inductions, and on 3/20 test animals 24 hours after the third induction. No reaction was noted on any test animal after challenge. Slight patchy erythema was noted on 2/10 naive control animals 24 hours after challenge. The positive control and positive naive control animals responded appropriately.

Conclusion:

1. **There is no indication that this product is a dermal sensitizer.**
2. **Classification**: Acceptable

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Chemical:	**Reynoutria sachalinensis**
	PC Code: 055809
HED File Code:	**41500 BPPD Tox/Chem**
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